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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/618,267

07/14/2003

Jonathan Schneck

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EXAMINER

DIBRINO, MARIANNE NMN

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1644

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01/21/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/618,267	Applicant(s) SCHNECK ET AL.	
	Examiner DiBrino Marianne	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 12-16, 48, 49 and 71-87 is/are pending in the application.
- 4a) Of the above claim(s) 16 and 71-87 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 12-15, 48 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's response filed 10/21/08 is acknowledged and has been entered.
2. Applicant is reminded of Applicant's election with traverse of Group I and species of solid support that is a bead, a T lymphocyte affecting molecule that is an antibody that specifically binds to CD28, an MHC class I complex comprising at least two fusion proteins, wherein a first fusion protein comprises a first MHC class I alpha chain and a first Ig heavy chain and wherein a second fusion protein comprises a second MHC class I alpha chain and a second Ig heavy chain, wherein the first and second Ig heavy chains associate to form the MHC class I molecular complex, wherein the MHC class I molecular complex comprises a first MHC class I peptide binding cleft and a second MHC class I peptide binding cleft in Applicant's response filed 7/31/06. The Examiner notes that the currently pending claims do not recite "at least two fusion proteins" nor that the first and second Ig heavy chains associate to form the MHC class I molecular complex.

Claims 1, 12-15, 48 and 49 are currently being examined.

3. For the purpose of prior art rejections, the filing date of the instant claims 1, 12-15, 48 and 49 is deemed to be the filing date of the 60/395,781 provisional parent application, *i.e.*, 7/12/02.

Applicant's statement in the response filed 10/21/08 on page 2 that the complex of Figure 1 of 60/395,781 comprise the entire Ig heavy chain, Figure 1 being labeled "Schematic of HLA-A2-Ig" is found persuasive in light of the disclosure in the instant specification (at [71], [72] and [160]) that "HLA-Ig" is described in U.S. Patent 6,268,411 (of record) and in light of the disclosure of '411 of HLA-Ig that comprise a full length Ig heavy chain.

4. Applicant's statement on page 4 of the response filed 10/21/08 that both the present application serial no. 10/618,267 and U.S. Patent 6,266,411 were at the time the invention of 10/618,267 were made, subject to an obligation of assignment to The Johns Hopkins University, has overcome the rejection of claims 1, 12-15, 48 and 49 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,268,411 B1 (of record) in view of Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08).

Applicant's other presented arguments on pages 3-4 of the response filed 10/21/08 are therefore moot, as the said rejection is withdrawn.

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5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1, 12-15, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) in view of Greten *et al* (PNAS USA 95: 7568-7573, 1998).

This is a new ground of rejection necessitated by Applicant's statement filed 10/21/08 as enunciated supra at item #4 of this Office Action.

Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) teach co-immobilized (on a rigid solid support that is a well on a microtiter plate) anti-CD28 antibodies along with class I MHC (murine K^d) /viral antigenic peptide complexes bound by anti-class I (anti-alpha 3) antibody, and use of the co-immobilized molecule to stimulate antigen-specific CD8⁺ T cells. Although Pardigon *et al* also teach stimulation of said T cells using each plate-bound molecule separately in series (MHC followed by anti-CD28) and also teach that signal 1 provided by MHC and signal 2 provided by anti-CD28 do not have to be delivered concomitantly to get optimal T cell activation, they teach sequential delivery in order to study the effect of such on potential situations encountered *in vivo* (see entire reference).

The primary reference differs from the instant invention in that the class I/peptide complexes of Pardigon *et al* are viral antigenic peptide-loaded single chain MHC class I fusion proteins, *i.e.*, peptide loaded into the peptide binding groove of a fusion protein comprising the MHC class I alpha chain and the β 2m light chain, that are bound by an antibody (comprising two full length heavy chains comprising a variable region, said antibody further comprising two light chains), the antibody binding to the alpha 3 domain of the MHC class I alpha chain. In contrast, the MHC class I alpha (*i.e.*, heavy) chains of the instant claims are each fused to an immunoglobulin heavy chain comprising a variable region.

Greten *et al* teach soluble viral peptide loaded human class I HLA-A2-Ig, *i.e.*, HLA-A2 extracellular region fused to IgG heavy chain said fusion protein in complex with β 2m light chain of HLA-A2 and the IgG light chain, resulting in a dimeric HLA-A2 (especially page 7569, column 1 at paragraph 3 and reference 20).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the rigid solid support taught by Pardigon *et al* by substituting the HLA-A2-Ig taught by Greten *et al*.

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One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a rigid solid support comprising an MHC complex that would be effective in stimulating human CD8⁺ T cells *in vitro*.

Claim 48 is included in this rejection because a microtiter plate is a preparation comprising a plurality of rigid solid supports, *i.e.*, wells of a microtiter plate.

Claim 49 is included in this rejection because the microtiter plates comprises PBS, a pharmaceutically acceptable carrier.

7. Claims 1, 12-15, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) in view of Greten *et al* (PNAS USA 95: 7568-7573, 1998) and WO 97/35991 A1 (of record).

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The primary reference differs from the instant invention in that the class I/peptide complexes of said reference are viral antigenic peptide-loaded single chain MHC class I fusion proteins, *i.e.*, peptide loaded into the peptide binding groove of a fusion protein comprising the MHC class I alpha chain and the β 2m light chain, that are bound by an antibody (comprising two full length heavy chains comprising a variable region, said antibody further comprising two light chains), the antibody binding to the alpha 3 domain of the MHC class I alpha chain. In contrast, the MHC class I alpha (*i.e.*, heavy) chains of the instant claims are each fused to an immunoglobulin heavy chain comprising a variable region.

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WO 97/35991 A1 teaches soluble divalent and multivalent heterodimeric analogs of proteins such as MHC class II-Ig that comprise two complete heavy chains of Ig. WO 97/35991 A1 further teaches that the soluble divalent analogs are used for inhibiting or decreasing immune responses, while the same soluble divalent analogs when immobilized on a substrate, are used to augment immune responses (especially abstract and page 9 at lines 18-31).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the rigid solid support taught by Pardigon *et al* by substituting the HLA-A2-Ig taught by Greten *et al*, particularly in light of the teaching that soluble divalent MHC-Ig such as the form taught by Greten *et al* comprising a fusion protein of the MHC extracellular region with an entire heavy chain Ig can be used to augment immune responses by immobilizing it on a substrate as taught by WO 97/35991 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a rigid solid support comprising an MHC complex that would be effective in stimulating human CD8+ T cells *in vitro*.

Claim 48 is included in this rejection because a microtiter plate is a preparation comprising a plurality of rigid solid supports, *i.e.*, wells of a microtiter plate.

Claim 49 is included in this rejection because the microtiter plates comprises PBS, a pharmaceutically acceptable carrier.

8. Claims 1, 12-15, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) in view of Dal Porto *et al* (PNAS USA 90: 6671-6675, IDS reference).

This is a new ground of rejection necessitated by Applicant's statement filed 10/21/08 as enunciated supra at item #4 of this Office Action

Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) teach co-immobilized (on a rigid solid support that is a well on a microtiter plate) anti-CD28 antibodies along with class I MHC (murine K^d) /viral antigenic peptide complexes bound by anti-class I (anti-alpha 3) antibody, and use of the co-immobilized molecule to stimulate antigen-specific CD8+ T cells. Although Pardigon *et al* also teach stimulation of said T cells using each plate-bound molecule separately in series (MHC followed by anti-CD28) and also teach that signal 1 provided by MHC and signal 2 provided by anti-CD28 do not have to be delivered concomitantly to get optimal T cell activation, they teach sequential delivery in order to study the effect of such on potential situations encountered *in vivo* (see entire reference).

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The primary reference differs from the instant invention in that the class I/peptide complexes of said reference are viral antigenic peptide-loaded single chain MHC class I fusion proteins, *i.e.*, peptide loaded into the peptide binding groove of a fusion protein comprising the MHC class I alpha chain and the β 2m light chain, that are bound by an antibody (comprising two full length heavy chains comprising a variable region, said antibody further comprising two light chains), the antibody binding to the alpha 3 domain of the MHC class I alpha chain. In contrast, the MHC class I alpha (*i.e.*, heavy) chains of the instant claims are each fused to an immunoglobulin heavy chain comprising a variable region.

Dal Porto *et al* teach soluble divalent class I MHC (Kd)-Ig, *i.e.*, the extracellular regions of the MHC class I fused to a complete heavy chain of Ig, the fusion proteins being bound by β 2m light chain and Ig light chain (materials and methods).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the rigid solid support taught by Pardigon *et al* by substituting the K^d-Ig taught by Dal Porto *et al* after antigen loading.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a rigid solid support comprising an MHC complex for convenience, *i.e.*, making a construct comprising a fusion protein of class I MHC heavy chain and an immunoglobulin light chain so as not to be dependent upon using an antibody that binds to the alpha 3 region of murine MHC class I molecules. In addition, a person of ordinary skill would have pursued other known options within his or her technical grasp in the pursuit of making a better construct, such as for instance in widening the conditions under which the construct could be used in screening, as antibody binding to the class I molecule would no longer be a consideration with an MHC class I-Ig fusion protein.

Claim 48 is included in this rejection because a microtiter plate is a preparation comprising a plurality of rigid solid supports, *i.e.*, wells of a microtiter plate.

Claim 49 is included in this rejection because the microtiter plates comprises PBS, a pharmaceutically acceptable carrier.

9. Claims 1, 12-15, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) in view of Dal Porto *et al* (PNAS USA 90: 6671-6675, IDS reference) and WO 97/35991 A1 (of record).

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The primary reference differs from the instant invention in that the class I/peptide complexes of said reference are viral antigenic peptide-loaded single chain MHC class I fusion proteins, *i.e.*, peptide loaded into the peptide binding groove of a fusion protein comprising the MHC class I alpha chain and the β 2m light chain, that are bound by an antibody (comprising two full length heavy chains comprising a variable region, said antibody further comprising two light chains), the antibody binding to the alpha 3 domain of the MHC class I alpha chain. In contrast, the MHC class I alpha (*i.e.*, heavy) chains of the instant claims are each fused to an immunoglobulin heavy chain comprising a variable region.

Dal Porto *et al* teach soluble divalent class I MHC (K^d)-Ig, *i.e.*, the extracellular regions of the MHC class I fused to a complete heavy chain of Ig, the fusion proteins being bound by β 2m light chain and Ig light chain (materials and methods).

WO 97/35991 A1 teaches soluble divalent and multivalent heterodimeric analogs of proteins such as MHC class II-Ig that comprise two complete heavy chains of Ig. WO 97/35991 A1 further teaches that the soluble divalent analogs are used for inhibiting or decreasing immune responses, while the same soluble divalent analogs when immobilized on a substrate, are used to augment immune responses (especially abstract and page 9 at lines 18-31).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the rigid solid support taught by Pardigon *et al* by substituting the K^d-Ig taught by Dal Porto *et al* after antigen loading, particularly in light of the teaching of WO 97/35991 A1 that soluble divalent MHC analogs may be used for augmenting an immune response when immobilized on a substrate.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a rigid solid support comprising an MHC complex for convenience, *i.e.*, making a construct comprising a fusion protein of class I MHC heavy chain and an immunoglobulin light chain so as not to be dependent upon using an antibody that binds to the alpha 3 region of murine MHC class I molecules. In addition, a person of ordinary skill would have pursued other known options within his or

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her technical grasp in the pursuit of making a better construct, such as for instance in widening the conditions under which the construct could be used in screening, as antibody binding to the class I molecule would no longer be a consideration with an MHC class I-Ig fusion protein.

Claim 48 is included in this rejection because a microtiter plate is a preparation comprising a plurality of rigid solid supports, *i.e.*, wells of a microtiter plate.

Claim 49 is included in this rejection because the microtiter plates comprises PBS, a pharmaceutically acceptable carrier.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1, 12-15, 48 and 49 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 6,268,411 B1 (IDS reference in the Form 1449 filed 7/14/03) in view of Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08).

Claims 1-34 of U.S. Patent No. 6,268,411 B1 are drawn to a composition comprising a complex comprising at least two chimeric proteins, wherein each chimeric protein comprises an MHC molecule, including an MHC class I alpha chain, and an Ig chain, including an Ig heavy chain that comprises a variable region, and wherein the complex

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further comprises immunoglobulin light chains and $\beta 2m$, and an antigenic peptide bound to the amino terminus of $\beta 2m$.

Claims 1-34 of U.S. Patent No. 6,268,411 B1 do not recite wherein the said composition is linked to a rigid solid support, nor wherein an antibody that binds CD28 is also linked to the rigid solid support.

Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) teach co-immobilized (on a rigid solid support that is a plate) anti-CD28 antibodies along with class I/peptide complexes bound by anti-class I (anti-alpha 3) antibody, and use of the co-immobilized molecule to stimulate antigen-specific CD8+ T cells. Although Pardigon *et al* also teach stimulation of said T cells using each plate-bound molecule separately in series (MHC followed by anti-CD28) and also teach that signal 1 provided by MHC and signal 2 provided by anti-CD28 do not have to be delivered concomitantly to get optimal T cell activation, they teach sequential delivery in order to study the effect of such on potential situations encountered *in vivo* (see entire reference).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have attached the complexes recited in claims 1-34 of U.S. Patent No. 6,268,411 B1 to a rigid solid support and to also include anti-CD28 antibodies as per the teaching of Pardigon *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a superior solid substrate comprising an MHC complex that would be effective in stimulating CD8+ T cells *in vitro*.

Applicant's argument in the response filed 10/21/08 has been fully considered, but is not persuasive.

Applicant may not obviate an obviousness-type double patenting rejection under 103(c).

12. Claims 1, 12-15, 48 and 49 stand directed to an invention not patentably distinct from claims 1-104 of commonly assigned U.S. Patent No. 6,268,411 B1 in view of Pardigon *et al* (J. Immunol. 2000, 164: 4493-4499, IDS reference in the Form 1449 filed 4/8/08) as enunciated above at item #7 of this Office Action.

The Examiner's remarks at #11 *supra*, apply herein.

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13. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,268,411 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

The Examiner's remarks at #11 supra, apply herein.

14. No claim is allowed.

15. Applicant's statement of common ownership (filed 10/21/08) resulting in the exclusion under 35 USC 103(c) of prior art reference US 6,266,411, as enunciated at item #4 of this Office Action supra, has necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

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If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Eileen B. O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
January 12, 2009

/G.R. Ewoldt/
Primary Examiner, Art Unit 1644